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(54) Disinfectant compositions

(57) A disinfectant composition particularly useful in skin cleansing, including when impregnated into a wipe, comprises:
a) an aqueous or mixed aqueous-alcoholic base;
b) an amine oxide or dioxide surfactant; and
c) at least one anti-microbial compound selected from:
(i) halogenated phenylalcohols;
(ii) p-hydroxybenzoic acid esters and their salts;
(iii) halogenated bis-phenols;
(iv) benzoic acid and its salts; and
(v) phenylphenols

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DISINFECTANT COMPOSITIONS

The present invention relates to disinfectant compositions which are particularly, but not exclusively, useful for skin cleansing.

Anti-microbial skin-cleansing compositions are well-known. In general they are based on an aqueous-alcoholic solution comprising one or more surfactants or wetting agents and one or more anti-microbial agents.

In view of practical considerations of safety, stability, odour, cost and sensitising action, the number of anti-microbial compounds available for this purpose is limited. Most widely used are hexachlorophene and quaternaries such as e.g. the cetyl trimethyl ammonium salts which combine surface-active and anti-microbial action.

It is also known to combine two or more anti-microbial agents in a number of cases resulting in synergistic effects.

In European patent application No. 0 024 031, a skin washing cleansing composition is described comprising a polyethyleneglycolester nonionic surfactant, a betaine or an amine oxide surfactant and optionally a basic amino or ammonium anti-microbial agent. The compositions are stated to have improved sudsing ability and significant anti-microbial action.

In particular, when applied in the user convenient form of impregnated wet wipes, conventional skin cleansing compositions often prove not to meet hygienic standards or to involve the use of anti-microbial quaternary ammonium compounds which due to their strong tendency to deposit on surfaces may have skin irritating effects when frequently used.

We have now discovered cleansing compositions having sufficient disinfecting power for application by wet wipes, sprays, lotions or other suitable means without the need of quaternary ammonium salt anti-microbial surfactants or agents. In particular it has now been found that the use of particular anti-microbial compounds in combination with an amine oxide and/or dioxide type of surfactant provides compositions showing synergistically increased anti-microbial effectiveness and being suitable for very frequent use.

Accordingly, the present invention provides a disinfectant composition suitable for use as a skin or other cleanser comprising in an aqueous or mixed aqueous-alcoholic base, an amine oxide and/or dioxide surfactant and an anti-microbial compound selected from the group of:

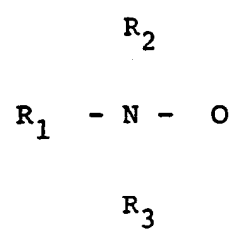
(i) halogenated phenylalkanols;

(ii) p-hydroxybenzoic acid esters and their salts;

(iii) halogenated bis-phenols;
(iv) benzoic acid and its salts; and
(v) phenylphenols.

The essential ingredients of the disinfectant cleansing compositions are the amine oxide and dioxide surfactants and one or more of specific anti-microbial compounds. In themselves both types of ingredients are conventional.

The amine oxide surfactant (when present) may for example have the structural formula:



wherein R_1 is a C_8-C_{18} alkyl group, preferably a C_{10}-C_{16} alkyl group, and R_2 and R_3 can be short-chain alkyl groups such as methyl, ethyl, n- and iso-propyl. R_2 and R_3 will generally be the same, but can differ if this is desired. Typical amine oxides suitable for the present invention are lauryl di-methyl amine oxide, mysistyl di-methyl amine oxide, cetyl dimethyl amine oxide, coconut dimethyl amine oxide, hardened tallow dimethyl amine oxide, hexadecyl dimethyl amine oxide, lauryl diethyl amine oxide and coconut diethyl amine oxide.

The amine dioxide surfactant (when present) may for example have the structural formula

wherein R_4 and R_5 are independently selected from those groups defined for R_2 and R_3 above and are preferably the same, most preferably both methyl;

R_6 is a C_{8-14} alkyl group, preferably having 9-11 carbon atoms; and

X is a suitable linking group, but is preferably chosen according to the parent diamine, and for example may be an alkylene linking group.

An especially preferred group of amine dioxides for use in the compositions of the present invention, comprises the N, N'-bis (C_{9-11} alkylmethyl) 1-6 hexanediamine dioxides.

In order to obtain the synergistic anti-microbial effects of the invention, amine oxide or dioxide concentrations can be used as low as 0.0005% by weight. In general, concentrations will lie in the range of from 0.001 to 10% by weight, concentrations of 0.1 to 2% by weight being preferred.

Referring to the aforesaid anti-microbial compounds of classes (1)-(5), suitable members of said p-hydroxybenzoic acid ester group (including salts thereof) are the lower alkyl esters, such as methyl-,

ethyl-, propyl- and n-butyl-p-hydroxybenzoate, (and salts of same) the latter ester and its salts being preferred.

Suitable members of said halogenated bis-phenols are the hydroxy halogenated derivatives of diphenyl methane, diphenylether and diphenylsulphide. Examples are dichlorophane (5,5'-dichloro-2,2'-dihydroxy diphenylmethane), bromochlorophane (3,3'-dibromo-5,5'-dichloro-2,2'-dihydroxy diphenylmethane), triclosan (2,4,4'-trichloro-2'-hydroxydiphenylether) and fentichlor (2,2'-dihydroxy-5,5'-dichlorodiphenylsulphide). Triclosan is the most preferred member.

Suitable members of the salts of benzoic acid are the alkali metal and earth alkali metal salts, sodium benzoate being most preferred.

Of the halogenated phenylalkanols, suitable members are the halogenated derivatives of benzylalcohol and phenylethylalcohol, in particular 2,4 dichlorobenzylalcohol.

Of the phenylphenols, in paticular o-phenylphenol has been found especially suitable.

The anti-microbial agent is included in an amount which provides effective disinfectant action. Dependent on the solubility and activity of the particular agent, such amount ranges from 0.001% to 10% by weight of the total composition. In particular, such amount ranges from 0.01 to 3% by weight and preferably lies within the range of from 0.05 to 0.5% by weight.

In general, the cleansing compositions of the present invention are aqueous or aqueous-alcoholic solutions. The alcohol may be included for reasons of both disinfection

and solubizing. The alcohol is a lower alcohol having up to four carbon atoms. In particular, ethanol and propanol is used within the range of from 1:1 to 1:3.

If included, the concentration of the alcohol component is at least 10% v/v and normally lies in the range of from 10 to 50% v/v. Preferred are aqueous-alcoholic solutions comprising ethanol or an ethanol/propanol mixture in a concentration of from 15 to 30% v/v.

Preferably, the compositions are buffered to skin compatible pH values in the range of from 3 to 6, in particular 4.5 to 5.5. This is conveniently effected using suitable buffering compositions, preferably added at concentrations of from 5 to 50m M, for example lactic acid/sodium lactate or citric acid/sodium citrate.

The composition of the invention may further comprise minor ingredients to improve its effectiveness and/or consumer acceptability, such as further surfactants, wetting agents, buffers, colouring agents and perfumes.

Although in particular suitable for application in the form of wet wipes, also other methods of application are suitable such as sprinkling or spraying thereof onto the surface to be cleansed, for example human skin or a hard surface.

The invention will further be illustrated by way of the following examples.

Example 1

Compositions on the basis of Empigen OB - ex Albright and Wilson (30% C_{13}-70% C_{11} alkyldimethylamine oxide) and dichlorobenzyl alcohol were tested for their antimicrobial action at pH 5.0 against Gram negative bacteria, as exemplified by Citrobacter freundii, Klebsiella edwardsii, Proteus mirabilis, Pseudomonas aeruginosa, and Salmonella cholerasuis, and against Gram positive bacteria as exemplified by Streptococcus faecalis, and against yeast as exemplified by Candida albicans.

Method:-

The organisms were grown up overnight in broth. Before use, the cells were centrifuged and resuspended to the same volume in 30mM sodium lactate buffer, pH 5.0. To 10ml test solution containing decreasing concentrations of either amine oxide or DCBA alone, were added 0.1 ml microbial suspension. After exactly 3 minutes, 1 ml of test suspension was added to 9ml quenching agent comprising an aqueous solution of 0.1% peptone, 0.1% sodium thiosulphate, 0.5% Tween 80 and 0.03% lecithin, the pH being 7.0. After serial dilution, the surviving organisms were counted by plating on Oxoid tryptone soy agar. In this way, the maximum level of the agent which would produce no or less than one decimal reduction in viable count was determined. The two agents were then combined at these concentrations and the test repeated with samples taken at 15 seconds and 3 minutes. Results are shown in Table 1.

Table 1

Antimicrobial effect of combinations of amine oxide and dichlorobenzyl alcohol.

Organism	Subinhibitory conc.* of agent used in the combination (ppm)		Log reduction in viable cells after exposure to the combination for-	
	AO	DCBA	15 sec.	3 min.
Citrobacter freundii	20	600	1.22	>5.6
Streptococcus faecalis	20	850	3.92	>5.5
Klebsiella edwardsii	30	750	3.00	>4.4
Salmonella cholerasuis	40	500	2.47	>4.1
Pseudomonas aeruginosa	40	800	3.90	>6.3
Proteus mirabilis	75	500	2.27	4.79
Candida albicans	200	1500	>4.52	-

* Conc. giving no or less than 1 log reduction in 3 min at 20°C

Examples 2-5

In these examples, the synergistic effect of amine oxide/biocide combinations according to the present invention was demonstrated by the following method. The level of each agent alone, that gave approximately two decimal reductions in the viable count of Escherichia coli was determined. The two agents were then combined in ratios of 4:0, 3:1, 2:2, 1:3, and 0:4 and the concentrations of the solutions to be mixed were such that a reduction of between one and two logs in viable count

would be predicted for either agent acting alone. Synergy is demonstrated when the mixtures result in fewer survivors. In each case the "amine oxide" was Empigen OB as defined above.

Example 2

Compositions on the basis of amine oxide and butyl para-hydroxybenzoic acid ester were tested for their anti-microbial action at pH=5 (20% ethanolic/citric acid buffer). Results are presented in Table 2.

Table 2

Final concentration in the mixture (Molar x 10^{-3})

Amine oxide	n-butyl p-hydroxy benzoate	Log. survivors
0	0	6.38
0.47	0	4.59
0.36	0.4	3.60
0.24	0.8	3.08
0.12	1.2	3.60
0	1.6	5.46

Example 3

Compositions on the basis of amine oxide and triclosan were tested for their anti-microbial action at pH=5 (20% ethanolic/citric acid buffer). Results as presented in Table 3.

Table 3

Final concentration in the mixture (Molar x 10^{-3})

Amine oxide	triclosan	Log. survivors
0	0	7.20
0.08	0	5.23
0.06	0.02	3.15
0.02	0.04	3.75
0.02	0.06	5.16
0	0.08	5.66

Example 4

Compositions on the basis of amine oxide and o-phenylphenol were tested for their anti-microbial action at pH=5 (20% ethanolic/citric acid buffer). Results are presented in Table 4.

Table 4

Final concentration in the mixture (Molar x 10^{-3})

Amine oxide	o-phenylphenol	Log. survivors
0	0	7.20
0.08	0	5.23
0.06	0.4	5.03
0.04	0.8	4.29
0.02	1.2	4.91
0	1.6	5.49

Example 5

Composition on the basis of amine oxide and benzoic acid were tested for their anti-microbial action at pH=5 (20% ethanolic/lactic acid buffer). The results are presented in Table 5.

Table 5

Final concentration in the mixture (molar x 10^{-3})

Amine oxide	Benzoic acid	Log survivors
0	0	6.05
0.16	0	4.03
0.12	2	1.00
0.08	4	3.85
0.04	6	5.97
0	8	6.09

Example 6 - Wipe Formulation

A base paper rectangle measuring 220mm x 270mm was impregnated with 5ml fluid of the following composition

Ethanol	20%
N-propanol	10%
Empigen OB	1%
DCBA	2%
Lactic acid	0.24%
Sodium lactate	0.06%
Deionised water	66.7%
to pH 5.0	

CLAIMS

1. A disinfectant composition comprising:

a) an aqueous or mixed aqueous-alcoholic base;
b) an amine oxide or dioxide surfactant; and
c) at least one anti-microbial compound selected from:

(i) halogenated phenylalcohols;
(ii) p-hydroxybenzoic acid esters and their salts;
(iii) halogenated bis-phenols;
(iv) benzoic acid and its salts; and
(v) phenylphenols

2. A composition according to claim 1, wherein the concentration of amine oxide or dioxide surfactant and that of the anti-microbial compound(s) are independently selected within the ranges of from 0.001 to 10% by weight.

3. A composition according to claim 2, wherein the concentration of amine oxide or dioxide surfactant is from 0.1 to 2% by weight and that of the anti-microbial compound(s) is from 0.01 to 3% by weight.

4. A composition according to any preceding claim when buffered to a pH in the range of from 3 to 6.

5. A wipe comprising a carrier sheet impregnated with a composition according to claim 4.